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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/464,039 | 12/15/1999 | Rachel Meyers | 5800-49 | 7067 |

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| EXAMINER |
|---|
| KAUSHAL, SUMESH |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | 16 |

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Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/464,039 | MEYERS, RACHEL | |
| | Examiner | Art Unit | |
| | Sumesh Kaushal Ph.D. | 1636 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *25 June 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *none*.

Claim(s) objected to: *none*.

Claim(s) rejected: *63-67,77-79 and 87-104*.

Claim(s) withdrawn from consideration: *none*.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☒ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). 4, 10

10.☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: Claims 63-67,77-79 and 87-104 stand rejected under 35 USC101, 35 USC 112(1) and 35 USC112(2) for the same reasons of record as set forth in the earlier official action mailed on the 03/25/02 and as repeated below :-

Claims 63-67, 77-79 and 87-104 stand rejected under 35 U.S.C. 101 because the claimed **invention lacks patentable utility**. The applicant argues that although the overall sequence similarity between T19954 (a hypothetical ribitol-dehydrogenase from C. elegans) and SEQ ID NO: is 41.7%, the T19954 polypeptide share approximately 64% local sequence similarity and approximately 74% local similarity between amino acid 2-276 of SEQ ID NO:7. The applicant further argues that nucleotide 27-386 of SEQ ID NO:7 share 99% sequence similarity with nucleotides 1694-2052 of A622988. The applicant further argues that considering PFAM analysis (functional domain consensus sequence) one skill in the art would conclude that the amino acids of SEQ ID NO:7 would have an alcohol dehydrogenase like activity (response, pages 2-4).

However, this is found unpersuasive because PFAM analysis revealed that 21612 matches with a top-scoring domain for ADH-short but with a low sequence similarity. It is known in the art that Alcohol dehydrogenase (ADH) constitutes a complex enzyme family with different forms and extensive multiplicity and the range of the biochemical reactions which can be catalyzed by individual ADH family members extremely wide and diverse (Duester, Eur. J. Biochem 267:4315-4324, 2000, see page 4316 table 1, 2, page 4317-4319). The specification fails to show a single working example that establishes that the SEQ ID NO: 8 which encodes the amino acid sequence of SEQ ID NO:7 is a member of Alcohol dehydrogenase (ADH) family, such as by any substantial sequence homology and/or functional assay of the protein. Considering the wide and diverse range of the ADH related substrates the instant specification fails to disclose what are the substrate for the polypeptide encoded by the nucleic acid as claimed. The specification even fails to characterize the instant invention as a particular subgroup of Alcohol dehydrogenase superfamily. Furthermore, it is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited SEQ ID NO(s) are simply computer-generated hypothesis because no biological function has been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene. Considering the state of art and guidance provided in the specification, the only immediate apparent utility for the instant invention would be its further scientific characterization of invention as claimed as a putative ADH protein like activity.

Claims 63-67, 77-79 and 87-104 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use the invention.**

The applicant argues that the specification provides sufficient guidance to allow one skill in the art to make nucleotide sequences falling within the structural limitations of the claims and determine whether these sequences encode polypeptides having functional limitations of the claims without undue experimentation. The applicant concluded that the specification as filed is enabled for the invention as claimed (response, pages 4-13).

However, this is found unpersuasive for the same reasons of record as set forth the lack of utility rejection above *(supra)*. Applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). The courts have clearly stated that: "A specification did not disclose what is well known in the art. See, e.g., Hybritech Inc. V. Monoclonal Antibodies, Inc., 802 F. 2d 1367, 1385, 231 USPQ 81, 94(Fed. Cir. 1986). *It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".* Genentech Inc. V. Novo Nordisk A/s, 42 USPQ2d 1005 (CAFC 1997). The specification fails to show a single working example that establishes that the SEQ ID NO: 8 which encodes the amino acid sequence of SEQ ID NO:7 is a member of Alcohol-dehydrogenase (ADH) family, such as by any substantial sequence homology and/or functional assay of the protein. Considering the wide and diverse range of the biochemical reactions, which can be catalyzed by individual ADH family members the instant specification fails to disclose what are the substrates for the polypeptide encoded by the nucleic acid as claimed. The specification fails provide any guidance how one skill in the art would use the invention as claimed when the function or the substrate of the polypeptide encoded by the nucleotide sequence of SEQ ID NO:8 are not known. Furthermore, the variants as claimed encompasses the conserved motifs that are germane to the ADH specific biological activity. The claimed invention is not enabled in view of lack of teachings in the specification as filed regarding what additional sequences may be added, deleted or substituted to those specifically disclosed, such that asserted utility discussed in the section 101 rejection above would be recognized as specific and/or substantial. At best specification as filed only teaches nucleic sequence of SEQ ID NO:8 which encodes the amino acid sequence of SEQ ID NO:7 and it is not even clear whether the SEQ ID NO:8 encodes any alcohol dehydrogenase like activity. *In addition screening of a biological activity based upon low sequence similarly and modification genetic sequence without sufficient guidance is not considered routine and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.* See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Considering the state of art and guidance provided in the specification, it is unclear how one skill in the art would use the invention as claimed when the biochemical activity of the polypeptides encoded by the claimed nucleotides in not known. Therefore, one

skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. The experimentation required would include scientific characterization of putative polypeptides as a member of Alcohol-dehydrogenase (ADH) family.

Claims 88-92 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, **had possession of the claimed invention.**

The applicant argues that invention as claimed meets the written description requirement as set forth in the 35 USC 112(1). The applicant further argues that structural features of sequence identity with SEQ ID NO: 7, hybridization with SEQ ID NO: 7 or the presence of subsequences of SEQ ID NO: 8 or amino acid sequence encoded by plasmid PTA-270, where the fragments have a given minimum length is sufficient to satisfy the written description requirement. The applicant further argues that SEQ ID NO:7 represent the genus as claimed (response, page 10-13).

However, this is found unpersuasive because the disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). The applicant even fails to point out where in the specification it is disclosed that the polypeptide encoded by the nucleic acid molecule of SEQ ID NO:8 have any alcohol dehydrogenase-like activity explicitly or implicitly as putatively consider by the applicant. The instant claims are drawn to a nucleotide sequence encoding a polypeptide having dehydrogenase activity, wherein the nucleotide has at least 70-90% sequence identity with nucleotide sequence of SEQ ID NO:8. The specification as fails to disclose any and all variant of human alcohol dehydrogenase comprising the nucleic acid sequence of SEQ 8, which encodes the amino acid sequences of SEQ ID NO:7. The specification discloses only one variant of ADH-like polypeptide within the scope of genus comprising the claimed SEQ ID NO:8. The specification proposes to discover other members of the genus using hybridization procedure. However, there is no description of mutational sites that exist in nature, and there is no description how the structure of identified nucleic acid sequences relates to the structure of any strictly neutral alleles. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USP2d 1481 at 1483. In Fiddes, claims directed to a mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In addition, possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claim 79 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The applicant argues that metes and bound of "instructions for use" would be clear to one skill in the art. However, this is found unpersuasive because it is unclear what the "instructions for use" would be in this context.

Scott D. Priebe

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PRIMARY EXAMINER